

REMARKS

Claims 1, 3, 6, 7 and 12-16 are pending. The Examiner is thanked for the courtesies extended during the interview of January 25th, 2010. In view of the Examiner's suggestions, Applicants amend claim 1 to specify a) the enzymes used for degradation, b) delete the language "or by effectors", and add a new claim 16 to specify types of cells that the complexes are administered to.

The support for claim 1 amendments may be found throughout the specification as filed and specifically at page 3, lines 1-2 and 10, page 6, line 25, page 7, line 17, page 8, lines 7 and 13, page 10, lines 7 and 16, page 12, line 21 and page 12, line 23 and page 7, line 8. The support for the new claim 16 may be found throughout the specification and specifically at page 2, lines 17-18, page 2, line 22 and page 6, line 17, page 6, lines 18-19, page 11, lines 19-20, page 9, line 17 and 23, Example 3, Example 4 and Example 6 of the published WO 2004/009134. Thus, no new matter has been added.

35 U.S.C. § 103

Claims 1, 3, 6, 7, 12 and 13 were rejected as obvious over the combination Kabalka et al. (Mag. Res. in Medicine, 1988, 8, 53, page 89-95, "Kabalka") as evidenced by Encyclopedia Britannica Article, "Reticuloendothelial System", in view of Ranney (U.S.5,155,215, "Ranney"). In view of the amendments to claim 1 and remarks presented below, Applicants request reconsideration and withdrawal of the rejection.

In order to establish obviousness, it is necessary, *inter alia*, to (i) determine the scope of the prior art and (ii) the differences between the claimed subject matter and that of the prior art. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). Furthermore, a *prima facie* finding of obviousness cannot be established when the "improvement is more than the predictable use of prior art elements according to their established functions." *KSR Int'l Co. v.*

Teleflex Inc., 127 S.Ct 1727, 1739 (2007). A reasonable expectation of success is required. MPEP 2143.02. Unexpected, *i.e.* surprising, results rebut a *prima facie* case of obviousness. MPEP 2144.09.

Applicants respectfully traverse the § 103(a) rejection because, for the reasons discussed below, the cited combination fails to teach or suggest all of the claim limitations.

The Cited Combination Fails to Teach or Suggest All of the Claim Limitations

Kabalka relates to gadolinium-labeled liposomes containing paramagnetic contrast agents which are specifically targeted for liver. Kabalka does not teach or suggest an instant method of cellular labeling wherein degradation of insoluble microparticles internalized into a targeted cell is necessary to form MR-imaging probes that would allow the registering of MRI images by T1-weighted sequences. Furthermore, Kabalka does not teach or suggest exploiting a specific enzymatic activity in a targeted cell in order to activate insoluble particles to a pool of water-soluble contrast agent units and to record MRI images reflecting the enzymatic expression and activity, wherein a specific enzyme is selected from a group consisting of β -galactosidase, esterase, proteinase, enzymes and lipase.

Ranney does not remedy the deficiency of Kabalka as evidenced by Encyclopedia Britannica Article. Ranney relates specific image-enhancing agents, contrast agents or spectral shift agents to enhance tissue or organ images. Ranney does not teach or suggest an instant method exploiting a specific enzymatic activity in a targeted cell in order to activate insoluble particles to a pool of water-soluble contrast agent units and to record MRI images reflecting the enzymatic expression and activity,

wherein a specific enzyme is selected from a group consisting of β -galactosidase, esterase, proteinase, enzymes and lipase. Therefore, for the above reasons, Applicants respectfully request withdrawal of the obviousness rejection over Kabalka as evidenced by Encyclopedia Britannica Article, "Reticuloendothelial System" in view of Ranney.

Conclusion

Therefore, for the above reasons, applicants submit that the presently pending claims are in condition for allowance and request the speedy issuance of a notice of allowability.

No fee, except the fee for a two month extension of time, is believed to be due for the filing of this Amendment and Response to non-Final Office Action. However, the Director is hereby authorized to charge any required fees and credit any overpayments to Deposit Account No. 50-0540.

Respectfully submitted,

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/Ilona Gont/
Ilona Gont, Reg. No. 58,714
Donald L. Rhoads, Reg. No. 34,705
KRAMER LEVIN NAFTALIS & FRANKEL LLP
1177 Avenue of the Americas
New York, NY 10036
(212) 715-9100 (telephone)
(212) 715-8000 (facsimile)